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Award Number:
W81XWH-11-2-0001

TITLE:
Role of Sleep Deprivation in Fear Conditioning and Extinction: Implications for Treatment of PTSD

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REPORT DATE:
October 2012

TYPE OF REPORT:
Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) October-2012		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 1 OCT 2011- 30 SEP 2012	
4. TITLE AND SUBTITLE Role of Sleep Deprivation in Fear Conditioning and Extinction: Implications for Treatment of PTSD				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-11-2-0001	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Sean P.A. Drummond, Ph.D.				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Veterans Medical Research Foundation San Diego, CA 92161				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, MD 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT PTSD is a growing concern for both active duty personnel and Veterans. Fear conditioning is implicated in the development of PTSD, while successful acquisition, consolidation, and recall of extinction memory are implicated in both the natural reduction of initial PTSD symptoms and as the mechanism underlying the most successful treatment for PTSD, Prolonged Exposure. In animal models, sleep deprivation has been shown to impair extinction memory, although this has never been directly tested in humans. This project is the first to examine the role of sleep and sleep loss in acquisition, consolidation, and generalization of extinction memory in humans. The goal of the second year was to have a cumulative enrollment of 53 subjects in the protocol. This goal was successful met.					
15. SUBJECT TERMS PTSD, sleep deprivation, fear conditioning, extinction memory, humans					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 5	19a. NAME OF RESPONSIBLE PERSON USAMPMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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Introduction

PTSD is a growing concern for both active duty personnel and Veterans. Fear conditioning is implicated in the development of PTSD, while successful acquisition, consolidation, and recall of extinction memory are implicated in both the natural reduction of initial PTSD symptoms and as the mechanism underlying the most successful treatment for PTSD, Prolonged Exposure. In animal models, sleep deprivation has been shown to impair extinction memory. Indirect evidence in humans also supports that notion, but it has never been tested directly in humans. Some of the most ubiquitous and distressing symptoms of PTSD are insomnia and nightmares. The resultant sleep deprivation may actually serve to perpetuate the disorder by interfering with treatments designed to promote extinction memories. Before this hypothesis can be tested in clinical populations, however, well-controlled experimental studies need to establish the exact role of sleep deprivation in extinction acquisition, consolidation, and recall in humans. This study will do just that. This is a mixed-effects study designed to examine the impact of 36 hours TSD on fear conditioning and consolidation (Aim 1), as well as extinction memory acquisition, recall, and generalization (Aim 2). A total of 60 subjects will participate across 3 years. Following recruitment and screening, subjects will spend 4 nights and days in the laboratory: a) adaptation to the lab (Night/Day0); b) normal sleep followed by fear memory acquisition (Night/Day1); c) sleep or TSD followed by fear recall and extinction memory acquisition (Night/Day2); and d) sleep or TSD followed by a test of extinction recall and generalization (Night/Day3). Group1 will receive sleep prior to each testing day, Group2 will be sleep deprived prior to Day2, and Group3 will be sleep deprived prior to Day3.

Body

This report covers the second year of the project. All milestones as set out in the Statement of Work (SOW) were successfully met. The goal of the second year was to enroll the bulk of our targeted subjects, so that we had a cumulative enrollment of 53 subjects, with approximately 44 who completed the full study and provided a full set of useable data (i.e., no artifacts in the physiological data). We successfully met this goal.

More specifically, at the end of Year 2 (30 Sept 2012), we had conducted initial phone screens on 648 individuals. Of those, 86 preliminarily qualified based on the phone screen, were able to make the time commitment required for the study, and were subsequently enrolled through signing informed consent. Of those 86, 52 subjects have completed the study. Of those not completing the study, 13 were excluded during the in-person intake (due mostly to being a non-responder to the startle paradigm), 12 withdrew for personal reasons, 6 were dropped due to revealing information after signing consent that made them ineligible, and 1 was withdrawn for protocol violations. Two were still in the middle of the study at the end of the fiscal year. Our subjects have included good diversity, with 24 women and 28 men, 17 Hispanic subjects, and 20 racial minorities (15 Asian, 2 Black, and 4 Mixed).

We have also remained up-to-date with all data processing, scoring, and archiving. There are a total of 47 subjects with 100% usable data, putting us above our target for the end of Year 2. We are currently exploring the data to determine if we can write a manuscript based on the relationship between sleep on the baseline nights and the fear conditioning paradigm. While such an analysis was not part of our original Aims, we believe this secondary aim could provide a valuable contribution to the literature.

Key Research Accomplishments

- Enrolled 86 subjects into the study, with 52 subjects fully completed and 47 subjects with fully usable data as of the end of Year 2

Reportable Outcomes

None

Conclusion

We successfully exceeded our milestone for Year 2 as outlined in the Statement of Work

References

N/A

Appendices

N/A

Supporting Data

N/A